Subpart A—Diphtheria Toxin for Schick Test

§ 650.1 Diphtheria Toxin for Schick Test.

The proper name of this product shall be Diphtheria Toxin for Schick Test, which shall be a preparation of a diphtheria toxin obtained from the growth of *Corynebacterium diphtheriae.*

§ 650.2 U.S. Standard preparation.

The U.S. Standard Diphtheria Toxin for Schick Test shall be used to determine the Schick test dose of the product. The Schick test dose of the standard is that amount of the standard that, when mixed with 0.001 unit of the U.S. Standard Diphtheria Antitoxin and injected intradermally in a guinea pig, will induce an erythematous reaction of 10 mm. in diameter.

§ 650.3 Manufacture of Diphtheria Toxin for Schick Test.

(a) *Propagation of bacteria.* The culture medium for propagation of the *Corynebacterium diphtheriae* for preparation of the parent toxin shall not contain ingredients known to be capable of producing allergenic effects in human subjects.

(b) *The parent toxin.* Diphtheria Toxin for Schick Test shall be prepared from a parent toxin which has been demonstrated to be stable and which contains no less than 400 minimum lethal doses per milliliter or 400,000 minimum reaction doses per milliliter. A minimum lethal dose is the smallest amount of toxin that will kill a guinea pig weighing approximately 250 gm. on the fourth day after its subcutaneous injection. A minimum reaction dose is that amount of toxin which when injected intradermally into a guinea pig induces an erythematous reaction 10 mm. in diameter.

§ 650.4 Potency test.

The dermal reactivity of each lot of the product shall be determined from the results of simultaneous guinea pig intradermal potency tests of the product under test and of the standard. The test shall be performed as follows:

(a) *Guinea pigs.* At least four healthy female guinea pigs shall be used, all of the same strain and each of a size that will permit a random distribution of eight intradermal injections. The hair shall be removed from the back and both sides of each guinea pig without producing abrasions of the skin. The denuded skin of each animal shall be sectioned into four equal areas at right angles to the vertebral column to provide two injection sites in each of the four areas, one on each side of the vertebra. The test is not valid if the guinea pigs do not show a graded response to the graded dilutions of the Schick test dose of the standard toxin.

(b) *Preparation of the test doses.* Four dilutions, two of the product under test and two of the U.S. Standard Diphtheria Toxin for Schick Test, shall be prepared in sterile buffered saline pH 7.4 containing 0.2 percent gelatin. The low and high dilutions of the standard shall be those amounts of a Schick test dose of the standard which in a dose of 0.1 ml. are capable of eliciting graded erythematous dermal reactions between 10 mm. and 20 mm. in diameter. The low and high dilutions of the Schick test dose of the toxin under test shall be the same as those of the standard toxin and estimated to have the same dermal reactivity.

(c) *Inoculation.* The low and high dilutions of the product (chart designation P_L and P_H) and the low and high dilutions of the standard (chart designations S_L and S_H) shall be injected intradermally in a volume of 0.1 ml. into each of the four guinea pigs according to either the following scheme, or in another scheme, provided it will permit comparable randomization of injection sites:

Area	Guinea Pig Number							
	1		2		3		4	
	Left	Right	Left	Right	Left	Right	Left	Right
A	S_L	S_L	S_H	S_H	P_L	P_L	P_H	P_H
B	S_H	S_H	S_L	S_L	P_H	P_H	P_L	P_L